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June 15, 2000

BY HAND DELIVERY

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, Maryland 20852

Re: FDA Docket No. 00D-1197; Guidance for Industry on Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act

Dear Sir or Madam:

Hyman, Phelps & McNamara P.C. ("HPM") submits these comments on the above-referenced FDA guidance document (hereinafter "Guidance"). The comments are submitted on behalf of a manufacturer of generic drugs.[1]

[1] In addition to addressing the merits of FDA's Guidance, these comments are also submitted to exhaust administrative remedies in the event of litigation.

00D-1197

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Summary

We support FDA's decision, expressed in the Guidance, to follow the determinations in TorPharm Inc. v. Shalala[2] and Mylan Pharm., Inc. v. Shalala[3] regarding the meaning of the term "court" in sections 505(j)(5)(B)(iii)(I) and (j)(5)(B)(iv)(II) of the Federal Food, Drug, and Cosmetic Act ("FDC Act"). These decisions found that FDA's earlier regulatory definition of "court" is inconsistent with the statute, and that the court decision which triggers abbreviated new drug application ("ANDA") approval prior to expiration of the 30-month automatic stay and the beginning of the 180-day exclusivity period is the decision of the first court that finds the patent in question to be invalid, unenforceable, or not infringed.[4]

We agree that FDA should revise its regulations to reflect this correct interpretation. We disagree, however, with the bifurcated approach described in the Guidance which applies the correct interpretation only to future ANDAs for which no other ANDA for the same reference listed drug has been submitted.

As discussed below, FDA should not draw any distinction between drugs for which an ANDA was submitted before the date of its Guidance, and drugs for which no ANDA was submitted until after the date of its Guidance. Instead, FDA should apply the correct statutory interpretation across the board to all ANDAs – pending and future – as the statute requires.

Alternatively, FDA should adopt a more narrowly tailored approach. In this approach, the agency would apply the correct interpretation of "court" to pending ANDAs

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2 TorPharm Inc. v. Shalala, C.A. No. 97-1925, 1997 U.S. Dist. LEXIS 21983 (D.D.C. Sept. 15, 1997); appeal withdrawn and remanded, 1998 U.S. App. LEXIS 4681 (D.C. Cir. Feb. 5, 1998); vacated, No. 97-1925 (D.D.C. Apr. 9, 1998).

3 Mylan Pharm., Inc. v. Shalala, 81 F. Supp. 2d 30 (D.D.C. 2000).

4 On March 31, 2000, one day after the Guidance was announced in the Federal Register (65 Fed. Reg. 16922 (Mar. 30, 2000)), the District Court for the District of Columbia issued another decision in the consolidated cases of Mylan Pharm., Inc. v. Henney, C.A. No. 99-862 and Pharmachemie B.V. v. Henney, C.A. No. 99-801 (hereinafter, "Pharmachemie") interpreting the word "court" in 21 U.S.C. §§ 355(j)(B)(5)(iii)(I) and (j)(B)(5)(iv) consistently with TorPharm and Mylan. See Mylan Pharm. Inc. v. Henney and Pharmachemie v. Henney, 94 F. Supp. 2d 36 (D.D.C. 2000).

for which there has not yet been a court decision in a patent infringement or declaratory judgment action brought under section 505(j)(5)(B)(iii) of the FDC Act. This approach would more closely comply with the statute, while providing the advantages the agency attempts to achieve in the Guidance, i.e., avoiding the disruption of the ANDA approval and 180-day exclusivity programs, or penalizing applicants who have made business decisions in good-faith reliance on FDA's existing regulations.

Finally, if the agency rejects both alternatives, it should accept waivers from first-filed applicants whose ANDAs containing paragraph IV certifications were submitted prior to the publication date of the Guidance. FDA's purpose in retaining the old rule is to protect first-filed applicants. It follows that those applicants have the right to refuse the agency's offer in favor of the statutory provisions as correctly interpreted.

I. FDA SHOULD APPLY THE NEW INTERPRETATION TO ALL ANDAS

The TorPharm, Mylan, and Pharmachemie courts found that the word "court" in sections 505(j)(5)(B)(iii)(I) and (j)(5)(B)(iv)(II) of the FDC Act clearly and unambiguously refers to the first court to decide that the patent is invalid, unenforceable or not infringed. The TorPharm, Mylan, and Pharmachemie courts also determined that FDA's regulation, 21 C.F.R. 314.107(e), which defines "court" as "the court that enters final judgment from which no appeal can be or has been taken," is based on an incorrect reading of the statute.

The Guidance adopts these determinations, but applies them only to ANDAs submitted after the date of the Guidance for which no other ANDA referencing the same listed drug has been submitted. In deciding that it will accept and apply the correct interpretation, FDA does not have discretion under the statute to continue applying the old, invalidated interpretation – even to ANDAs already on file. The agency, in devising the bifurcated approach described in the Guidance, was clearly trying to ensure that the first-filed ANDA applicant does not suddenly lose a portion or all of its exclusivity period. However, the determination of whether the first-filed applicant has relied on FDA's old interpretation such that an inequity would result from application of the new interpretation to that applicant is not one FDA is authorized to make as part of its implementation of the statute. Nothing in the FDC Act permits the agency to make exceptions to the ANDA effective date provisions of the statute on the ground that applying those provisions would produce unjust results by reason of the FDA's previous interpretations. Nor does FDA have general authority to mitigate the perceived inequitable effects of the FDC Act by suspending the statute's operation in particular cases, or classes of cases, even when those effects are attributable to the agency's own error. Achieving equity is an authority granted to courts, not administrative agencies.

Moreover, assuming FDA had the authority to suspend the statute to avoid unacceptable consequences to those that relied on the agency's incorrect interpretation, whether that should be done in a given case is a fact-specific analysis more appropriately decided in the context of a concrete factual setting than by speculative judgment in the abstract. Therefore, FDA should uniformly apply the correct, new interpretation to all pending and future ANDAs.

II. FDA SHOULD ADOPT A MORE NARROWLY TAILORED "BRIGHT LINE" APPROACH

If FDA does not apply the new interpretation of "court" to all ANDAs, it should revise its "bright line" approach to one that is more narrowly tailored.

The Guidance characterizes FDA's "bright line" approach as follows:

> The new definition of *court* will apply to certain ANDAs submitted after the publication of this guidance. Specifically, the new definition will be used for approval and exclusivity determinations for ANDAs containing a paragraph IV certification where the ANDA cites a reference listed drug for which no other ANDA containing a paragraph IV certification has been submitted.

Guidance at 4. In other words, all ANDAs filed before March 30, 2000, as well as ANDAs filed after March 30, 2000 which reference a listed drug for which an ANDA containing a paragraph IV certification was submitted before March 30, 2000, will still be subject to the old interpretation of "court" in FDA's existing regulation, 21 C.F.R. § 314.107(e).

As the basis for this approach, the Guidance states:

> Th[e] new interpretation of the statute may substantially change the value of the 180-day exclusivity. As Judge Roberts recognizes in the Mylan opinion, applicants who have made certain business decisions in good faith reliance upon an FDA regulation should not be penalized for their actions. For example, the potential change in the value of exclusivity may have considerable effect upon an ANDA applicant's willingness to file a paragraph IV certification to a patent and to undertake the effort and expense of litigating a patent infringement suit. This may be particularly true for patent challenges that are seen as risky, but for which the possible award of a full exclusivity was an adequate incentive. Judge Roberts also noted that based upon FDA's interpretation of the statute, ANDA

> applicants have held products off the market even after a victory in the district court.
>
> The Agency believes that an implementation plan for the new definition of *court* that recognizes the industry's reliance on the previous definition and establishes a *bright line* for ANDAs affected by the new definition will minimize the disruption to the ANDA approval and 180-day exclusivity programs. Moreover, the Agency believes that this approach will lessen the likelihood that ANDA applicants will sue the Agency alleging that they, like Geneva in the Mylan case, relied in good faith on the Agency's regulation and would be irreparably injured by application of the new interpretation to pending ANDAs.

Guidance at 4-5.

In Mylan, Geneva Pharmaceuticals, Inc. ("Geneva") was the first applicant to file an ANDA containing a paragraph IV certification referencing both tablet and capsule forms of Abbott Laboratories' ("Abbott's") Hytrin (terazosin hydrochloride) product.

Mylan Pharmaceuticals, Inc. ("Mylan") was the second applicant to file an ANDA containing a paragraph IV certification referencing Hytrin capsules only. Abbott sued both Geneva and Mylan for patent infringement – Geneva with respect to the tablet formulation, and Mylan with respect to the capsule formulation. Although Geneva was not sued with respect to its capsule formulation, and the 30-month statutory stay applied only to its tablet formulation, Geneva refrained from marketing the capsules out of fear that doing so would expose the company to liability for infringement before the tablet litigation was resolved. Mylan, 81 F. Supp. 2d at 34-35.

On September 1, 1998, the district court declared Abbott's patent invalid with respect to Hytrin tablets. On July 1, 1999, the Federal Circuit affirmed on appeal. Pursuant to FDA's regulation, which interpreted the term "court" to mean "the court that enters final judgment from which no appeal can be or has been taken," first-to-file Geneva then became eligible for approval and marketing of its tablet product subject to a 180-day exclusivity period. The invalidation of Abbott's patent also cleared the way for Geneva to commence marketing its capsule product without fear of liability for infringement. Accordingly, on August 13, 1999, Geneva began marketing both its tablets and capsules. Since Geneva's capsule formulation was not the subject of any patent infringement litigation, FDA interpreted Geneva's exclusivity period for the capsules to begin on the date of their first commercial marketing. Id. at 35.

While the litigation between Abbott and Geneva was ongoing, Mylan filed its ANDA referencing Hytrin capsules, and was sued by Abbott for patent infringement. On March 4, 1999, the district court held that the patent was invalid on the basis of collateral estoppel from its finding in the Abbott-Geneva litigation. Since Mylan was not the first applicant to file, however, the agency declined to approve Mylan's application until Geneva's exclusivity for its capsules expired, 180 days after Geneva first began to market the capsules. Id.

Mylan sued the agency, claiming that FDA's refusal to grant final approval of its ANDA pending the expiration of Geneva's exclusivity period for the capsules was unlawful. Mylan contended that Geneva's 180-day exclusivity period should have been measured from the date of the district court's decision in Mylan's favor, because it was the first court decision invalidating Abbott's patent with respect to Hytrin capsules. Mylan requested a preliminary injunction directing FDA to approve its ANDA immediately, claiming that it had suffered and would continue to suffer irreparable losses in revenue as a result of FDA's refusal to approve the ANDA. Id. at 35-36.

Although the court agreed with Mylan on the merits, and determined that the word "court" in FDC Act § 505(j)(5)(B)(iv) includes the decision of a district court, Judge Roberts declined to grant the requested injunctive relief on the grounds that it would unfairly deprive Geneva of its remaining exclusivity after Geneva had relied in good faith on FDA's regulation for the decision to withhold its capsules from the market pending appellate review. Specifically, Judge Roberts explained,

> it would be inequitable to penalize Geneva for its reliance after it had endured six years of litigation with Abbott which ultimately cleared the way for other generic manufacturers, including Mylan, to market their generic Hytrin products. The balance of harms therefore weighs against granting Mylan the injunctive relief it seeks.

Id. at 44-45.

FDA's reliance on Mylan makes clear that the agency is primarily concerned with injustice to first-filed ANDA applicants as a result of applying the new interpretation in situations where action has already been taken (or, in the case of FDA final approval,

withheld) in reliance on the old interpretation.[5] However, FDA's "bright line" approach is broader than it needs to be or should be to address this concern.

For example, application of the old interpretation makes no sense when there is only one ANDA applicant for a listed drug as of the date of FDA's Guidance, and this first-filed applicant has been sued by the patent holder, but the case is still pending at the district court level. If the new interpretation of "court" is applied, and a district court decision is issued favoring the applicant, the applicant's exclusivity period will begin as of the date of the court decision. In addition, assuming that all substantive approval requirements are met, the first-filed applicant's ANDA will also be eligible for final approval as of the date of the court decision. The applicant will not lose anything it was entitled to under the statute as correctly interpreted as a result of prior reliance (by the applicant or FDA) on the old interpretation.[6] On the contrary, application of the new interpretation in this situation would benefit the first-filed applicant, later-filed applicants, and the public by permitting generic drugs to enter the market, and competition to begin, sooner.

The same would be true if more than one ANDA application were pending for the same reference listed drug as of the Guidance's publication date, and one or more of the later-filed applicants were also sued for infringement by the patent owner, provided that all of the lawsuits were still pending at the district court level.

Only in situations where the district court has already ruled in favor of the first-filed applicant, and the patent-owner has appealed, or its right to appeal has not yet expired, does the first-filed applicant stand to lose some portion of its exclusivity entitlement when the new interpretation is applied. This was the concern reflected by Judge Roberts in Mylan, and which motivated FDA's prospective-only approach in the Guidance. In that scenario, FDA already would have delayed approval of the first-filed applicant's ANDA pending expiration of the right to appeal, the conclusion of the appeal in the applicant's

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5 Although later-filed ANDA applicants and NDA holders may also have an interest in the effect of FDA's approach, only first-filed ANDA applicants are at risk of losing their exclusivity benefit as a result of enforcement of the new interpretation following reliance on the old interpretation.

6 Even if other ANDAs are submitted after the publication date of the Guidance (or a revised Guidance clarifying how the Mylan decision will be applied), the first-filed applicant would already be on notice that it should not prospectively rely on FDA's existing regulation with regard to commencement of its exclusivity period, and that the exclusivity period could be triggered by the decision of a court in an infringement lawsuit involving a later-filed application.

favor, or expiration of the 30-month stay, based on the old interpretation. Subsequent application of the new interpretation recognizing the decision of the district court as the exclusivity trigger would result in commencement (and perhaps expiration) of the first-filed applicant's exclusivity period before FDA approves the application, thus precluding the applicant from the opportunity to market its drug during its exclusivity period.

A more narrowly tailored "bright line" approach would better meet FDA's objective of giving maximum effect to the new interpretation, while avoiding disruption of the ANDA approval and 180-day exclusivity programs, or penalizing applicants who have made business decisions in good-faith reliance upon FDA's existing regulations. Such an approach could be stated as follows:

> The new interpretation of "court" will be used for approval and exclusivity determinations with respect to all pending and future ANDAs containing a paragraph IV certification for the same reference listed drug, provided that, as of the date of publication of FDA's revised Guidance, there has been no court decision favoring the first-filed ANDA applicant with respect to that reference listed drug in a patent infringement or declaratory judgment action brought under section 505(j)(5)(B)(iii) of the FDC Act.

This approach would protect drug companies such as Geneva in the Mylan case, which would otherwise lose at least a portion of their exclusivity period. But it would also enable companies to benefit from application of the new interpretation to pending ANDAs, and would accelerate public access to generic drugs.

III. FDA SHOULD IMPLEMENT A WAIVER MECHANISM ALLOWING FIRST-FILED APPLICANTS TO OPT OUT OF THE PROTECTION AFFORDED BY THE GUIDANCE

If FDA applies its current "bright line" approach, or adopts a modified approach such as the one described above, not all first-filed ANDA applicants necessarily will be in favor of the protection afforded by the bifurcated approach. Since only the first-filed applicant is subject to an inequitable result from the application of the new interpretation after actions already have been taken in reliance on the old interpretation, FDA should permit the first-filed applicant to accept or decline the protection afforded by the bifurcated approach through the establishment of a waiver system. If the first-filed applicant declines application of the old interpretation, FDA should apply the new interpretation to all pending and future ANDAs containing paragraph IV certifications for the same reference listed drug.

Again, this approach would protect drug companies like Geneva in the Mylan case, while at the same time enabling companies to benefit from application of the new interpretation and accelerating public access to generic drugs.

IV. CONCLUSION

FDA should apply the correct interpretation of "court" across the board to all pending and future ANDAs. Alternatively, FDA should modify its "bright line" approach to one that is more closely tailored to the concern expressed in the Guidance. If FDA rejects both of these proposals, or adopts the proposed (or some other) modified approach to bifurcated implementation, the agency should implement a waiver procedure to allow first-filed ANDA applicants to opt out of the protection FDA seeks to afford them through prolonged enforcement of the old, invalidated interpretation.

Sincerely,

Thomas Scarlett

TS/sas